In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

1. (Amended) A method for modifying, in an animal, metabolism of glucagon-like peptide 1 (GLP-1), comprising administering to the animal a composition including one or more inhibitors of a dipeptidylpeptidase which inactivates GLP-1, which inhibitor(s) inhibit(s) the dipeptidylpeptidase proteolysis of GLP-1 at a $K_i$ of 1 nM or less.

2. A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit DPIV-mediated proteolysis having a Ki of 1 nM or less.

3. (Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit the proteolysis of glucagon-like peptide 1 (GLP-1) having a Ki of 1 nM or less.

4. (Amended) A method for treating Type II diabetes, comprising administering to an animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) which have a $K_i$ of 1 nM or less.

5. (Amended) The method of claim 1, wherein the dipeptidylpeptidase is DPIV.

6. (Amended) The method of claim 2 or 3, wherein the protease inhibitor is an inhibitor of DPIV.

7. (Amended) The method of claim 2 or 3, wherein administering the inhibitor reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.



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8. (Amended) The method of claim1. 2, 3 or 4, wherein the inhibitor has an $EC_{50}$ for modification of glucose metabolism which is at least one order of magnitude less than its $EC_{50}$ for immunosuppression.

9. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an $EC_{50}$ for inhibition of glucose tolerance in the nanomolar or less range.

10. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an $EC_{50}$ for immunosuppression in the μM or greater range.

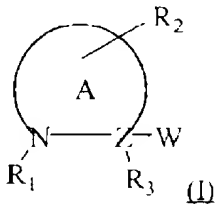
11. (Amended) The method of any of claim 1, 2, 3 or 4, wherein the inhibitor has a $K_i$ for DPIV inhibition of 0.5 nM or less.

12. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is peptidomimetic of a peptide selected from the group consisting Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

13. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has a molecular weight less than 7500 amu.

14. (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is administered orally.

15 (Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is represented by the general Formula I;



(I)

wherein,

A represents a 4-8 membered heterocycle including a N and a Cα carbon;

Z represents C or N;



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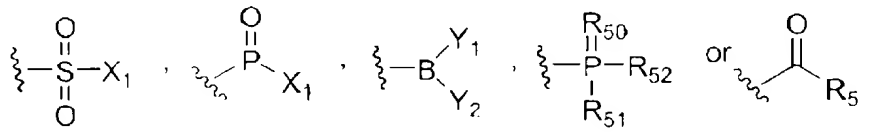
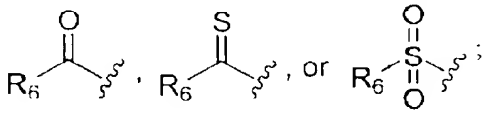
W represents -CN, -CH=NR$_5$,



R$_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



R$_2$ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-lower alkyl, -(CH$_2$)$_m$-O-lower alkenyl, -(CH$_2$)$_n$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-lower alkyl, -(CH$_2$)$_m$-S-lower alkenyl, or -(CH$_2$)$_n$-S-(CH$_2$)$_m$-R$_7$;

if Z is N, then R$_3$ represents a hydrogen;

if Z is C, then R$_3$ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-lower alkyl, -(CH$_2$)$_m$-O-lower alkenyl, -(CH$_2$)$_n$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-lower alkyl, -(CH$_2$)$_m$-S-lower alkenyl, or -(CH$_2$)$_n$-S-(CH$_2$)$_m$-R$_7$;

R$_5$ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X$_1$)(X$_2$)X$_3$, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-alkyl, -(CH$_2$)$_m$-O-alkenyl, -(CH$_2$)$_m$-O-alkynyl, -(CH$_2$)$_m$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-alkyl, -(CH$_2$)$_m$-S-alkenyl, -(CH$_2$)$_m$-S-alkynyl, -(CH$_2$)$_m$-S-(CH$_2$)$_m$-R$_7$, -C(O)C(O)NH$_2$, or -C(O)C(O)OR'$_7$;

R$_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-alkyl, -(CH$_2$)$_m$-O-alkenyl, -(CH$_2$)$_m$-O-alkynyl, -(CH$_2$)$_m$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-alkyl, -(CH$_2$)$_m$-S-alkenyl, -(CH$_2$)$_m$-S-alkynyl, -(CH$_2$)$_m$-S-(CH$_2$)$_m$-R$_7$,



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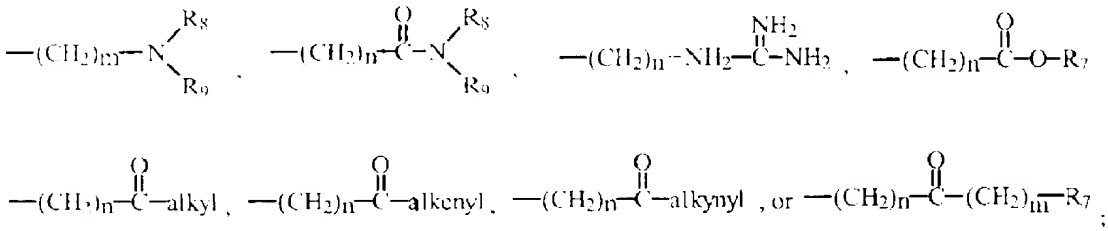

$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocyclyl;

$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

$R_{50}$ represents O or S;

$R_{51}$ represents $N_3$, SH, $NH_2$, $NO_2$ or $OR'_7$;

$R_{52}$ represents hydrogen, a lower alkyl, an amine, $OR'_7$, or a pharmaceutically acceptable salt, or $R_{51}$ and $R_{52}$ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

$X_1$ represents a hydrogen or a halogen, or a hydroxyl;

$X_2$ and $X_3$ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

16. (Amended) The method of claim 15, wherein,

W represents -CN, $-CH=NR_5$,



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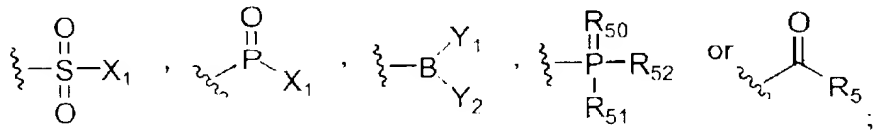

$R_5$ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$-alkyl, $-(CH_2)_n-O$-alkenyl, $-(CH_2)_n-O$-alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$-alkyl, $-(CH_2)_n-S$-alkenyl, $-(CH_2)_n-S$-alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

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$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$Y_1$ and $Y_2$ can independently or together be hydroxyl, , an alkoxyl, or, taken together, Y1 and $Y_2$ are connected via a ring having from 5 to 8 atoms in the ring structure which can be hydrolyzed to hydroxy groups;

$R_{50}$ represents O or S;

$R_{51}$ represents $N_3$, SH, $NH_2$, $NO_2$ or $OR'_7$;

$R_{52}$ represents hydrogen, a lower alkyl, an amine, $OR'_7$, or a pharmaceutically acceptable salt, or $R_{51}$ and $R_{52}$ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

$X_1$ represents a hydrogen or a halogen, or a hydroxyl;

$X_2$ and $X_3$ each independently represent a hydrogen or a halogen.

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

17. (Amended) The method of claim 15, wherein the ring A is represented by the formula



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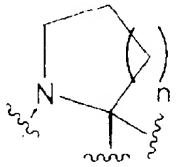
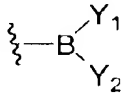
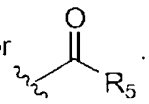
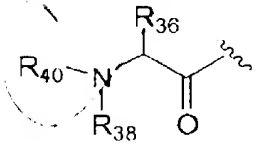


wherein,

n is an integer of 1 or 2.

18. (Amended) The method of claim 15, wherein W represents  or  .

19. (Amended) The method of claim 15, wherein $R_1$ represents



$R_{36}$ represents a small hydrophobic group and $R_{38}$ is hydrogen, or, $R_{36}$ and $R_{38}$ together form a 4-7 membered heterocycle including the N and the Cα carbon, as defined for A above; and

$R_{40}$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

20. (Amended) The method of claim 15, wherein $R_2$ is absent, or represents a small hydrophobic group.

21. (Amended) The method of claim 15, wherein $R_3$ is a hydrogen, or a small hydrophobic group.

22. (Amended) The method of claim 15, wherein $R_5$ is a hydrogen, or a halogenated lower alkyl.

23. (Amended) The method of claim 15, wherein $X_1$ is a fluorine, and $X_2$ and $X_3$, if halogens, are fluorine.



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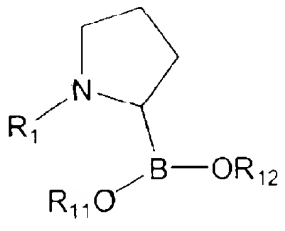
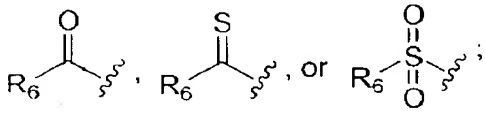
24. (Amended) The method of claim 15, wherein the inhibitor is represented by the general Formula (II):

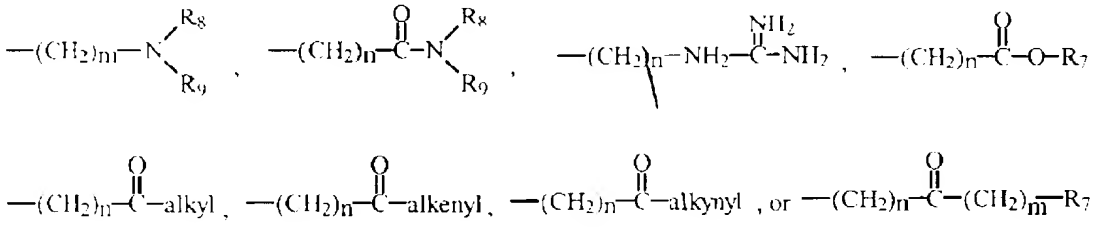


(II)

wherein,

$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or  ;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-$R_7$,



$R_7$ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, -$(CH_2)_m$-$R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m$-$R_7$,
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

$R_{11}$ and $R_{12}$ each independently represent hydrogen, an alkyl, or a pharmaceutically acceptable salt, or $R_{11}$ and $R_{12}$ taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;



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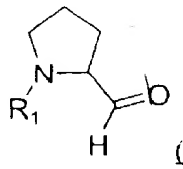
m is zero or an integer in the range of 1 to 8; and

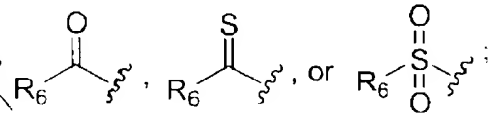
n is an integer in the range of 1 to 8.

25. (Amended) The method of claim 15, wherein the inhibitor is represented by the general Formula III,

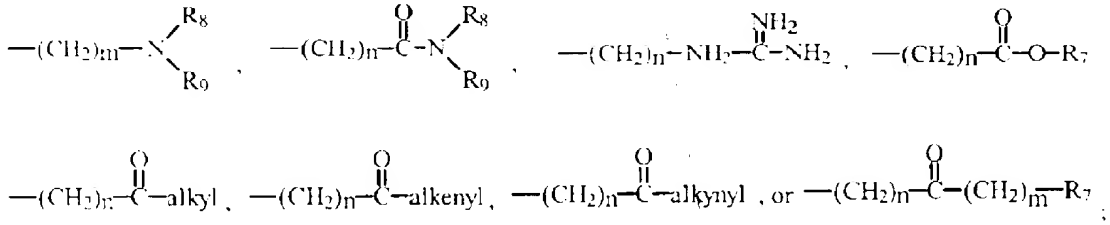


(III)

wherein,

$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,  ;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-$R_7$,



$R_7$ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, -$(CH_2)_m$-$R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m$-$R_7$.



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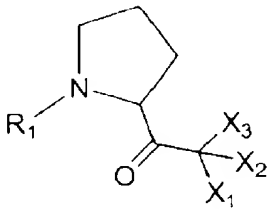
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

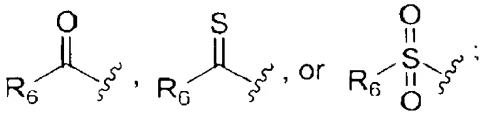
m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

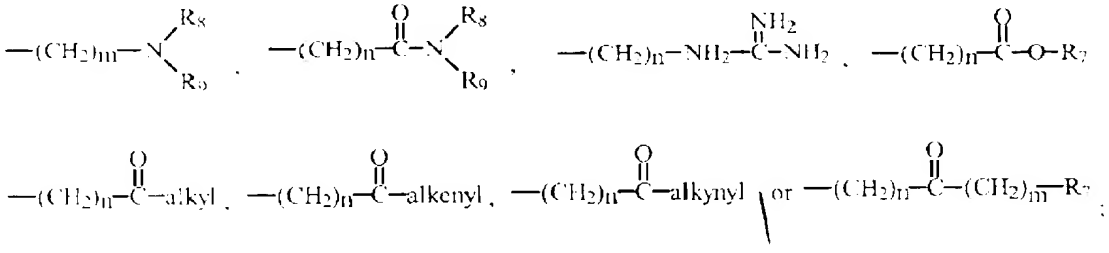
26. (Amended) The method of claim 15, wherein the inhibitor is represented by the general formula:



wherein,

$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,  ;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-$R_7$,



$R_7$ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;



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$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, C(=O)-alkenyl, -C(=O)-alkynyl, $-C(=O)-(CH_2)_m-R_7$,

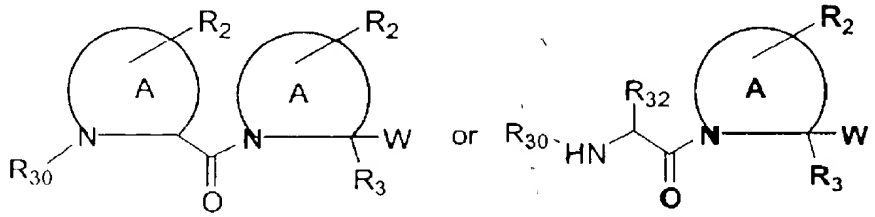
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

$X_1$, $X_2$ and $X_3$ each represent a hydrogen or a halogen; and

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

27. (Amended) The method of claim 15, wherein the inhibitor is represented by the general Formulae IVa or IVb :

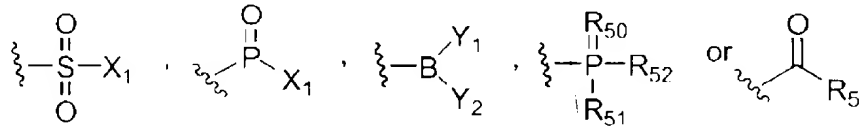



(IVa) (IVb)

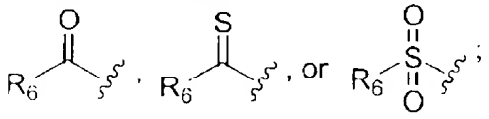
wherein,

A represent a 4-8 membered heterocycle including a N and a Cα carbon;

W represents -CN, $-CH=NR_5$,




$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group,




$R_3$ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, -



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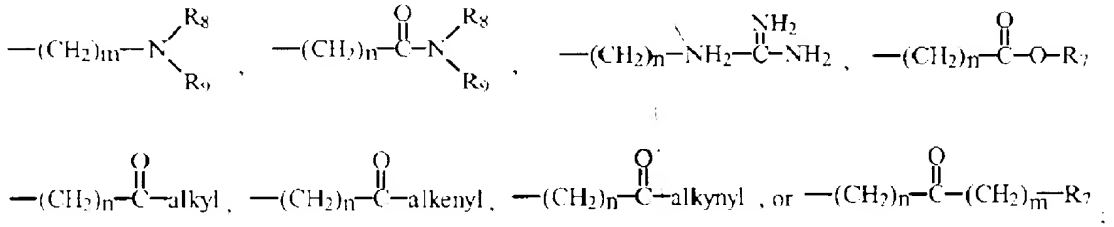
$(CH_2)_m$-O-lower alkyl, $-(CH_2)_m$-O-lower alkenyl, $-(CH_2)_n$-O-$(CH_2)_m$ $R_7$, $-(CH_2)_m$-SH, $-(CH_2)_m$-S-lower alkyl, $-(CH_2)_m$-S-lower alkenyl, or $-(CH_2)_n$-S-$(CH_2)_m$-$R_7$;

$R_5$ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m$-$R_7$, $-(CH_2)_n$-OH, $-(CH_2)_n$-O-alkyl, $-(CH_2)_n$-O-alkenyl, $-(CH_2)_n$-O-alkynyl, $-(CH_2)_n$-O-$(CH_2)_m$-$R_7$, $-(CH_2)_n$-SH, $-(CH_2)_n$-S-alkyl, $-(CH_2)_n$-S-alkenyl, $-(CH_2)_n$-S-alkynyl, $-(CH_2)_n$-S-$(CH_2)_m$-$R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m$-$R_7$, $-(CH_2)_m$-OH, $-(CH_2)_m$-O-alkyl, $-(CH_2)_m$-O-alkenyl, $-(CH_2)_m$-O-alkynyl, $-(CH_2)_m$-O-$(CH_2)_m$-$R_7$, $-(CH_2)_m$-SH, $-(CH_2)_m$-S-alkyl, $-(CH_2)_m$-S-alkenyl, $-(CH_2)_m$-S-alkynyl, $-(CH_2)_m$-S-$(CH_2)_m$-$R_7$,



$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m$ $R_7$, C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or C(=O) $(CH_2)_m$-$R_7$,
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;
$R_{32}$ is a small hydrophobic group;
$R_{34}$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group;

$R_{50}$ represents O or S;



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$R_{51}$ represents $N_3$, SH, $NH_2$, $NO_2$ or $OR'_7$;

$R_{52}$ represents hydrogen, a lower alkyl, an amine, $OR'_7$, or a pharmaceutically acceptable salt, or $R_{51}$ and $R_{52}$ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

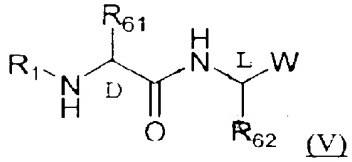
$X_1$ represents a hydrogen or a halogen, or a hydroxyl;

$X_2$ and $X_3$ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

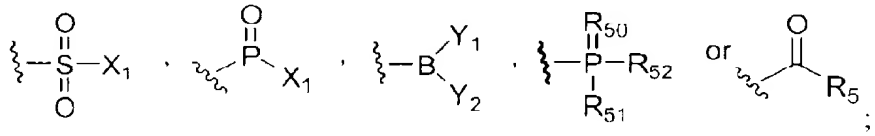
28. 28. (Amended) The method of claim 1, 2, 3, 4, or 15, wherein the inhibitor is represented by the general Formula V:



(V)

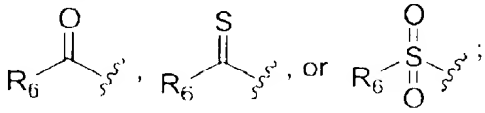
wherein,

W represents a functional group which reacts with an active site residue of the targeted protease, selected from -CN, -CH=$NR_5$,



;

$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group, or



;

$R_3$ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a



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nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-lower alkyl, -$(CH_2)_m$-O-lower alkenyl, -$(CH_2)_n$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-lower alkyl, -$(CH_2)_m$-S-lower alkenyl, or -$(CH_2)_n$-S-$(CH_2)_m$-$R_7$;

$R_5$ represents H, an alkyl, an alkenyl, an alkynyl, -$C(X_1)(X_2)X_3$, -(CH2)m-$R_7$, -(CH2)n-OH, -(CH2)n-O-alkyl, -(CH2)n-O-alkenyl, -(CH2)n-O-alkynyl, -(CH2)n-O-(CH2)m-$R_7$, -(CH2)n-SH, -(CH2)n-S-alkyl, -(CH2)n-S-alkenyl, -(CH2)n-S-alkynyl, -(CH2)n-S-(CH2)m-$R_7$, -$C(O)C(O)NH_2$, or -$C(O)C(O)OR'_7$;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, or -$(CH_2)_m$-S-$(CH_2)_m$-$R_7$;

$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R_{61}$ and $R_{62}$, independently, represent small hydrophobic groups;

$Y_1$ and $Y_2$ can independently or together be OH or an alkoxyl, or, taken together, Y1 and $Y_2$ are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

$R_{50}$ represents O or S;

$R_{51}$ represents $N_3$, SH, $NH_2$, $NO_2$ or $OR'_7$;

$R_{52}$ represents hydrogen, a lower alkyl, an amine, $OR'_7$, or a pharmaceutically acceptable salt, or $R_{51}$ and $R_{52}$ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

$X_1$ represents a halogen;

$X_2$ and $X_3$, independently for each occurrence, represent a hydrogen or a halogen;



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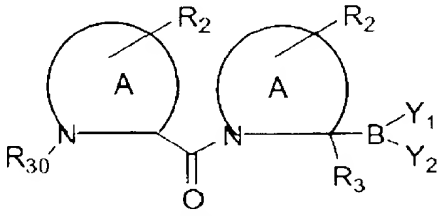
m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

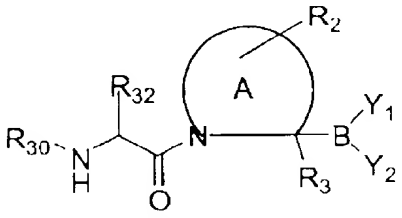
29. (Amended) A method for modfiying, in an animal, metabolism of peptide hormone, comprising administering to the animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) with $K_i$s of 1 nM or less, which peptide hormone is selected from glucagon-like peptide 2 (GLP-2), growth hormone-releasing factor (GHRF), vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), pituitary adenylate cyclase activating peptide (PACAP), gastric inhibitory peptide (GIP), helodermin, Peptide YY and neuropeptide Y.

30. (Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

31. (Amended) The method of claim 30, wherein the boronyl peptidomimetic is represented in the general Formulae VIa c,

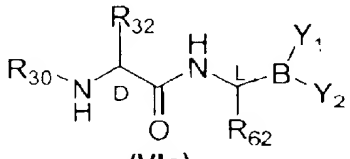


(VIa)



(VIb)

or



(VIc)

wherein,



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each A independently represents a 4-8 membered heterocycle including an N and a Cα carbon;

$R_2$ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

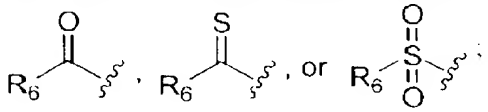
$R_3$ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, or $-(CH_2)_m-S-(CH_2)_m-R_7$;

$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocyclyl;

$R_{30}$ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



$R_{32}$ represents lower alkyl or halogen;



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$Y_1$ and $Y_2$ can independently or together be OH or an alkoxyl, or, taken together, $Y_1$ and $Y_2$ are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

$R_{62}$ represents lower alkyl or halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

85 cont'd.

32. (Amended) The method of claim 31, wherein administering the boronyl peptidomimetic reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

33. (Amended) The method of claim 31, wherein the boronyl peptidomimetic has an $EC_{50}$ for modification of glucose metabolism which is at least one order of magnitude less than its $EC_{50}$ for immunosuppression.

34. (Amended) The method of claim 31, wherein the boronyl peptidomimetic has an $EC_{50}$ for inhibition of glucose tolerance in the nanomolar or less range.

35. (Amended) The method of claim 31, wherein the boronyl peptidomimetic has an $EC_{50}$ for immunosuppression in the μM or greater range.

36. (Amended) The method of claim 31, wherein the boronyl peptidomimetic is administered orally.

37. (Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition comprising a peptidomimetic boronyl inhibitor wherein the peptide to be mimicked is selected from Pro-Pro, Ala-Pro, and (D) Ala-(L)-Ala.

Please add the following new claims:



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38. (New) A method for modifying glucose metabolism in a glucose intolerant animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit DPIV-mediated proteolysis.

39. (New) A method for modifying glucose metabolism in a glucose intolerant animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit the proteolysis of glucagon-like peptide 1 (GLP-1).

40. (New) A method for modfiying, in a glucose intolerant animal, metabolism of a peptide hormone, comprising administering to the animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) with in an amount sufficient to increase the plasma half-life of the peptide hormone, which peptide hormone is selected from glucagon-like peptide 2 (GLP-2), growth hormone-releasing factor (GHRF), vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), pituitary adenylate cyclase activating peptide (PACAP), gastric inhibitory peptide (GIP), helodermin, Peptide YY and neuropeptide Y.

41. (New) A method for modifying glucose metabolism of a glucose intolerant animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

42. (New) The method of any of the claims 38-41 wherein, the glucose intolerance in the animal is a result of a deletion or disruption of the gene encoding for a glucagon type peptide.

43. (New) The method of claim 42 wherein, the glucagon type peptide is GLP-1 or GLP-2.

44. (New) The method of claim 38, wherein the dipeptidylpeptidase is DPIV.

45. (New) The method of claim 38 or 39, wherein the protease inhibitor is an inhibitor of DPIV.



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46. (New) The method of claim 38 or 39, wherein administering the inhibitor reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

47. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has an $EC_{50}$ for modification of glucose metabolism which is at least one order of magnitude less than its $EC_{50}$ for immunosuppression.

48. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has an $EC_{50}$ for inhibition of glucose tolerance in the nanomolar or less range

49. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has an $EC_{50}$ for immunosuppression in the μM or greater range.

50. (New) The method of any of claim 38, 39, 40, or 41, wherein the inhibitor has a $K_i$ for DPIV inhibition of 0.5 nM or less.

51. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

52. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor has a molecular weight less than 7500 amu.

53. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is administered orally.

54. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is represented by the general Formula VII;



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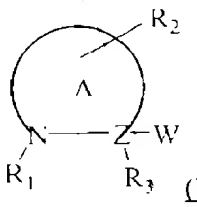


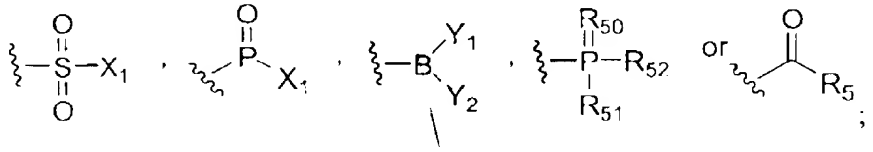
(VII)

wherein,

A represents a 4-8 membered heterocycle including a N and a Cα carbon;

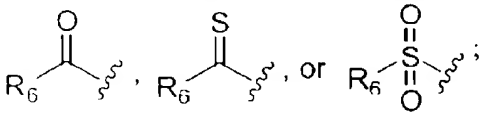
Z represents C or N;

W represents -CN, -CH=NR$_5$,



;

R$_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group,



;

R$_2$ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$ OH, -(CH$_2$)$_m$-O-lower alkyl, -(CH$_2$)$_m$-O-lower alkenyl, -(CH$_2$)$_n$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-lower alkyl, -(CH$_2$)$_m$-S-lower alkenyl, or -(CH$_2$)$_n$-S-(CH$_2$)$_m$-R$_7$;

if Z is N, R$_3$ represents a hydrogen;

if Z is C, R$_3$ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-lower alkyl, -(CH$_2$)$_m$-O-lower alkenyl, -(CH$_2$)$_n$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-lower alkyl, -(CH$_2$)$_m$-S-lower alkenyl, or -(CH$_2$)$_n$-S-(CH$_2$)$_m$-R$_7$;



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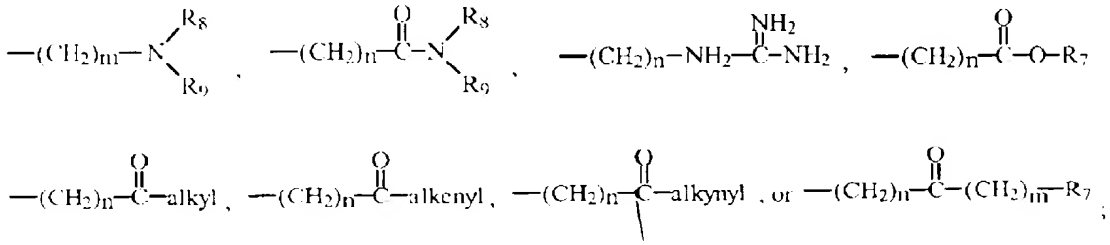
$R_5$ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$-alkyl, $-(CH_2)_n-O$-alkenyl, $-(CH_2)_n-O$-alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$-alkyl, $-(CH_2)_n-S$-alkenyl, $-(CH_2)_n-S$-alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, $-(CH_2)_m-S-(CH_2)_m-R_7$,



$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(=O)$-alkyl, $-C(=O)$-alkenyl, $-C(=O)$-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

$R_{50}$ represents O or S;

$R_{51}$ represents $N_3$, SH, $NH_2$, $NO_2$ or $OR'_7$;

$R_{52}$ represents hydrogen, a lower alkyl, an amine, $OR'_7$, or a pharmaceutically acceptable salt, or $R_{51}$ and $R_{52}$ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;



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$X_1$ represents a hydrogen or a halogen, or a hydroxyl;

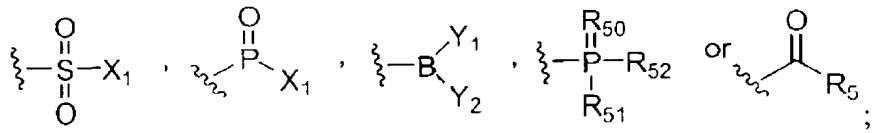
$X_2$ and $X_3$ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

55. (New) The method of claim 54, wherein,

W represents -CN, -CH=$NR_5$,



$R_5$ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$-alkyl, $-(CH_2)_n-O$-alkenyl, $-(CH_2)_n-O$-alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$-alkyl, $-(CH_2)_n-S$-alkenyl, $-(CH_2)_n-S$-alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$Y_1$ and $Y_2$ can independently or together be hydroxyl, or taken together $Y_1$ and $Y_2$ are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

$R_{50}$ represents O or S;

$R_{51}$ represents $N_3$, SH, $NH_2$, $NO_2$ or $OR'_7$;

$R_{52}$ represents hydrogen, a lower alkyl, an amine, $OR'_7$, or a pharmaceutically acceptable salt, or $R_{51}$ and $R_{52}$ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;



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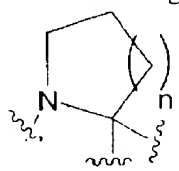
$X_1$ represents a hydrogen or a halogen, or a hydroxyl; and

$X_2$ and $X_3$ each represent a hydrogen or a halogen.

56. (New) The method of claim 54, wherein the ring A is represented by the formula

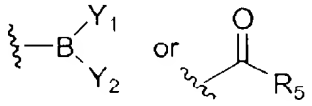


wherein,

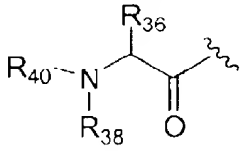
Bb cont

n is an integer of 1 or 2.

57. (New) The method of claim 54, wherein W represents



58. (New) The method of claim 54, wherein $R_1$ represents



$R_{36}$ represents a small hydrophobic group and $R_{38}$ is hydrogen, or, $R_{36}$ and $R_{38}$ together form a 4-7 membered heterocycle including the N and the Cα carbon, as defined for A above; and

$R_{40}$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

59. (New) The method of claim 54, wherein $R_2$ is absent, or represents a small hydrophobic group.



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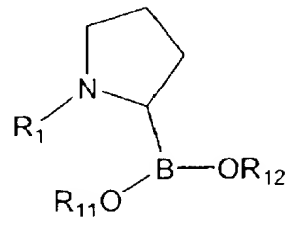
60. (New) The method of claim 54, wherein $R_3$ is a hydrogen, or a small hydrophobic group.

61. (New) The method of claim 54, wherein $R_5$ is a hydrogen, or a halogenated lower alkyl.

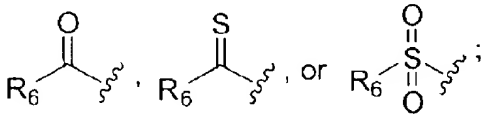
62. (New) The method of claim 54, wherein $X_1$ is a fluorine, and $X_2$ and $X_3$, if halogens, are fluorine.

63. (New) The method of claim 54, wherein the inhibitor is represented by the general Formula (VIII):

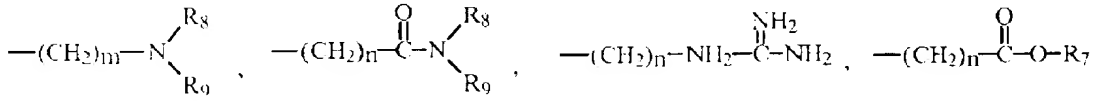


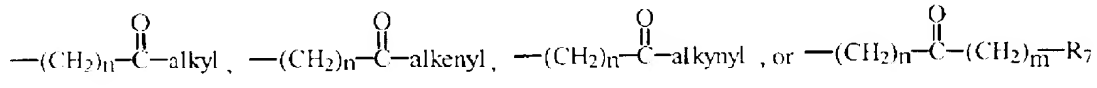
(VIII)

wherein,

$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,  ;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-$R_7$,





$R_7$ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;



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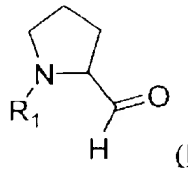
$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

$R_{11}$ and $R_{12}$ each independently represent hydrogen, an alkyl, or a pharmaceutically acceptable salt, or $R_{11}$ and $R_{12}$ taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

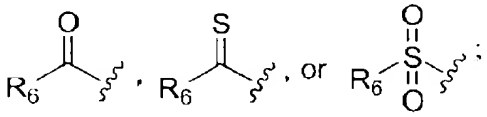
m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

64. (New) The method of claim 54, wherein the inhibitor is represented by the general Formula IX,



(IX)

wherein
$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,  ;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, $-(CH_2)_m-S-(CH_2)_m-R_7$,



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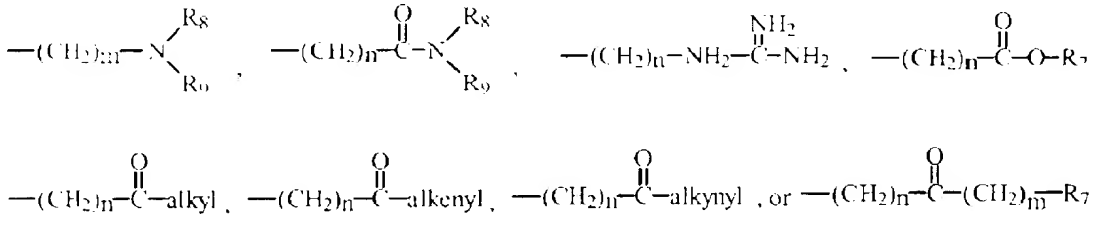


$R_7$ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

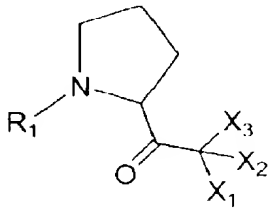
$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,

or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

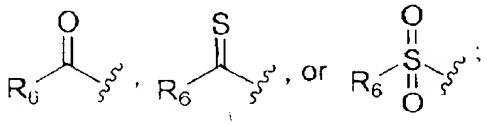
m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

65. (New) The method of claim 54, wherein the inhibitor is represented by the general formula:



wherein,

$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,  ;

$R_4$ represents a small hydrophobic group;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-



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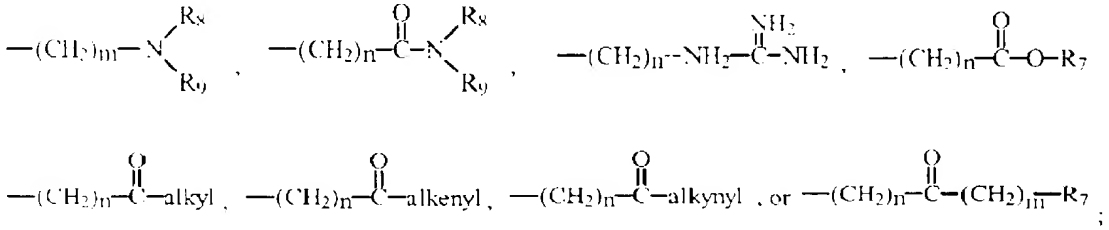
alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, $-(CH_2)_m-S-(CH_2)_m-R_7$,



$R_7$ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(=O)$-alkyl, $-C(=O)$-alkenyl, $-C(=O)$-alkynyl, $-C(=O)-(CH_2)_m-R_7$,

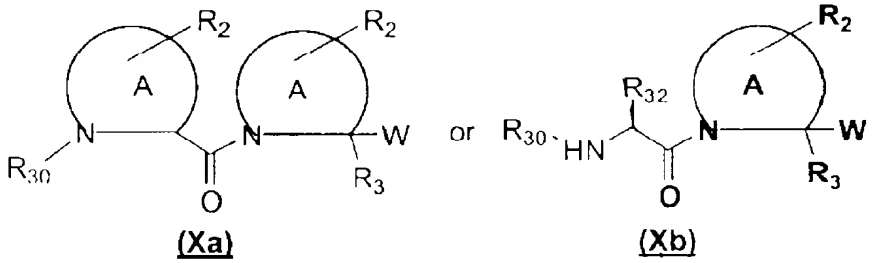
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

$X_1$, $X_2$ and $X_3$ each represent a hydrogen or a halogen; and

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

66. (New) The method of claim 54, wherein the inhibitor is represented by the general Formulae Xa or Xb :



(Xa) or (Xb)

wherein,

A represents a 4-8 membered heterocycle including a N and a Cα carbon;



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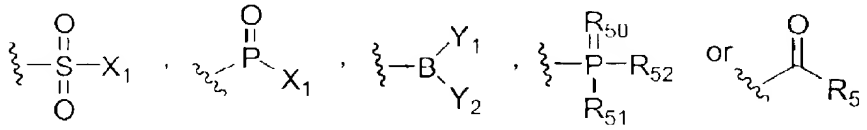
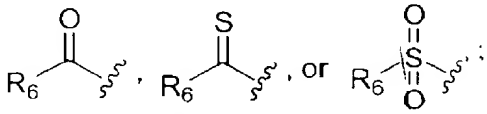
W represents -CN, -CH=NR$_5$,



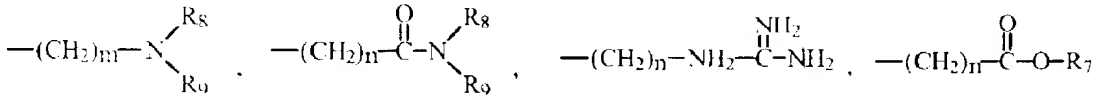
$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group,

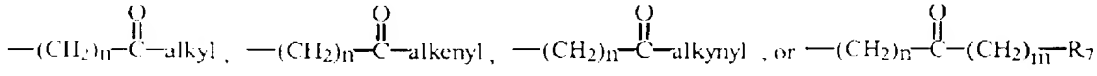


$R_3$ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-lower alkyl, -$(CH_2)_m$-O-lower alkenyl, -$(CH_2)_n$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-lower alkyl, -$(CH_2)_m$-S-lower alkenyl, or -$(CH_2)_n$-S-$(CH_2)_m$-$R_7$;

$R_5$ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -$C(X_1)(X_2)X_3$, -$(CH_2)_m$-$R_7$, -$(CH_2)_n$-OH, -$(CH_2)_n$-O-alkyl, -$(CH_2)_n$-O-alkenyl, -$(CH_2)_n$-O-alkynyl, -$(CH_2)_n$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_n$-SH, -$(CH_2)_n$-S-alkyl, -$(CH_2)_n$-S-alkenyl, -$(CH_2)_n$-S-alkynyl, -$(CH_2)_n$-S-$(CH_2)_m$-$R_7$, -C(O)C(O)$NH_2$, or -C(O)C(O)OR'$_7$;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-$R_7$,







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$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R'_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R_8$ and $R_9$ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,
or $R_8$ and $R_9$ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;
$R_{32}$ is a small hydrophobic group;
$R_{30}$ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group;

$R_{50}$ represents O or S;

$R_{51}$ represents $N_3$, SH, $NH_2$, $NO_2$ or $OR'_7$;

$R_{52}$ represents hydrogen, a lower alkyl, an amine, $OR'_7$, or a pharmaceutically acceptable salt, or $R_{51}$ and $R_{52}$ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

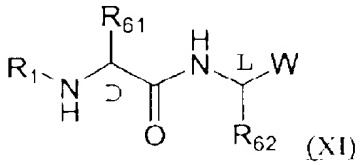
$X_1$ represents a hydrogen or a halogen, or a hydroxyl;

$X_2$ and $X_3$ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

67. (New) The method of claim 38, 39, 40, or 41, wherein the inhibitor is represented by the general Formula XI:



(XI)

wherein,



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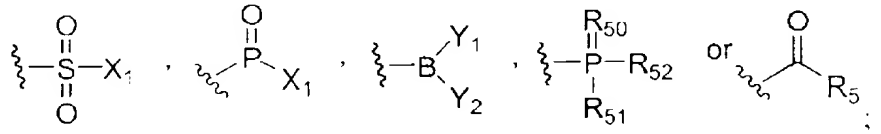
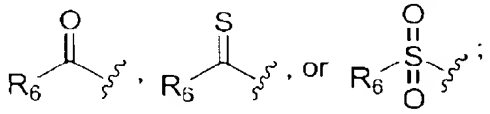
W represents a functional group which reacts with an active site residue of the targeted protease selected from -CN, -CH=NR$_5$,



$R_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



$R_3$ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-lower alkyl, -$(CH_2)_m$-O-lower alkenyl, -$(CH_2)_n$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-lower alkyl, -$(CH_2)_m$-S-lower alkenyl, or -$(CH_2)_n$-S-$(CH_2)_m$-$R_7$;

$R_5$ represents H, an alkyl, an alkenyl, an alkynyl, -$C(X_1)(X_2)X_3$, -$(CH_2)$m-$R_7$, -$(CH_2)$n-OH, -$(CH_2)$n-O-alkyl, -$(CH_2)$n-O-alkenyl, -$(CH_2)$n-O-alkynyl, -$(CH_2)$n-O-$(CH_2)$m-$R_7$, -$(CH_2)$n-SH, -$(CH_2)$n-S-alkyl, -$(CH_2)$n-S-alkenyl, -$(CH_2)$n-S-alkynyl, -$(CH_2)$n-S-$(CH_2)$m-$R_7$, -C(O)C(O)$NH_2$, or -C(O)C(O)OR'$_7$;

$R_6$ represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-$R_7$, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-$R_7$, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, or -$(CH_2)_m$-S-$(CH_2)_m$-$R_7$;

$R_7$ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'$_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

$R_{61}$ and $R_{62}$, independently, represent small hydrophobic groups;



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